



UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office

Address: COMMISSIONER OF PATENTS AND TRADEMARKS

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/408,761	09/29/99	DALE	

DIANNA L DEVORE
BOZICEVIC FIELD AND FRANCIS LLP
200 MIDDLEFIELD ROAD, SUITE 200
MENLO PARK, CA 94025

HM22/1122

EXAMINER LUNDGREN, J

ART UNIT 1031	PAPER NUMBER
------------------	--------------

DATE MAILED:

11/22/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/408,761

Applicant(s)

DALE, RODERIC M. K.

Examiner

Jeffrey S. Lundgren

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 September 2000.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 34-46 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 34-46 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5.
- 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other: _____

DETAILED ACTION

Specification

1. The objection to the specification in the Office Action mailed on December 23, 1999, is maintained, as a statement from Applicant indicating that the CRF and paper copy of the sequence listing are identical as required by 37 CFR 1.821 through 1.825, is absent.

Claim Rejections - 35 USC § 112

2. The rejection of claims 1-9, and 15 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention in the Office Action mailed December 23, 1999, is withdrawn for the reasons argued by Applicant in the response received on September 5, 2000.
3. The rejection of claims 1-9, and 14-15 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention in the Office Action mailed December 23, 1999, is withdrawn for the reasons argued by Applicant in the response received on September 5, 2000.

Claim Rejections - 35 USC § 102

4. The rejection of claims 1-9, and 14 under 35 U.S.C. 103(a) as being unpatentable over Dwyer et al. (U.S. Patent No. 5,986,083, November 16, 1999) in view of Miller et al. (WO 94/15619, 21 July, 1994) in the Office Action mailed December 23, 1999, are overcome by Applicant's amendments in the response received on September 5, 2000.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claims 34, and 37-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over McGall et al. (EP 0 742 287 A2, November 13, 1996) in light of Miller et al. (WO 94/15619, July 21, 1994) in view of Lipshutz et al. (U.S. Patent No. 6,013,440, January 12, 2000).

Claims 34, and 37-46 are drawn to an array comprising a substrate with a plurality of oligonucleotides, wherein the oligonucleotides are modified at the 2' position. The physicochemical properties of the oligonucleotides are that oligonucleotides are more stable under acidic conditions, and have a greater binding affinity to their

respective complement compare to the affinity of the same sequence without the 2' position modification to its respective complement. Further, the array is designed so that the T_m of any given oligonucleotide sequence bound to its complement sequence, is substantially the same as the T_m of any other oligonucleotide sequence bound to its complement sequence. The array may be comprised of oligonucleotides having an average length of about 80 to 300 nucleotides or 100 to 200 nucleotides, wherein the sequences of different distinct area are different, and the sequences of a distinct area are the same, and the array may comprise from 2 to 10^9 distinct areas.

McGall discloses an array of oligonucleotides attached to solid substrates, wherein the arrays are modified at the 2' position, and have an increased binding affinity to their complementary oligonucleotide sequence, such as either DNA or RNA. The modification to the oligonucleotides comprises alkoxy modifications, such as methoxy, ethoxy, propoxy (see formula on page 1). The array may comprise up to 10^6 distinct areas.

Although McGall teaches the chemical structure modification to oligonucleotides immobilized to an array, McGall does not teach that an inherent property of 2' modified oligonucleotides, such as those modified with 2' methoxy, are acid resistant. McGall also fails to teach designing the array such that that the T_m of any given oligonucleotide sequence bound to its complement sequence, is substantially the same as the T_m of any other oligonucleotide sequence bound to its complement sequence. McGall does not teach array with oligonucleotides in the range of 80 to 300 nucleotides in length.

Miller discloses that oligonucleotides modified with 2' methoxy groups are more stable to degradation under acidic conditions. Similar to Applicant's experimental findings (see Examples 2-4 of the instant application), Miller shows through a controlled experiment that the protected oligonucleotides are 175x more stable than the phosphodiester deoxyadenosine analogs as a result of the 2' O-methoxy group (see Tables I & II, and descriptions thereof; starting on page 19), and states (page 19):

"The results clearly demonstrate that the 2' O-methyladenosinyl methylphosphonates are vastly more stable (175x) than either of the phosphodiester deoxyadenosine or methylphosphonate deoxyadenosine analogs."

Lipshutz discloses an array comprising oligonucleotides, wherein the length of the oligonucleotide of the array are most preferably 150 nt long (column 5, lines 25-41). Further, the oligonucleotides of the array are selected such that the T_m of each oligonucleotide sequence of each distinct area is within a given allowable T_m interval, most preferably the allowable T_m interval range is 5 °C (see column 11, line 58 to column 12, line 65). In doing so, an array with a uniform T_m is created, which increases target specificity of the between the array-based oligonucleotide the complementary oligonucleotide which hybridizes to said array-based oligonucleotide, concurrently reducing mismatch pairing.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to restrict the oligonucleotides of the array to an allowable/uniform T_m range as taught by Lipshutz, with the array of McGall, because of the advantages of increase array specificity for target oligonucleotides. Furthermore, the skilled artisan would recognize that longer oligonucleotides of the array, such as those of Lipshutz,

would be advantageous for longer targets, such as more full-length cDNAs. Therefore, the invention as a whole was *prima facie* obvious at the time the invention was made.

7. Claims 35 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over McGall and Lipshutz (and Miller) as applied to claims 34, and 37-46 above, and further in view of King et al. (U.S. Patent No. 5,376,528, December 27, 1994).

Claims 35 and 36 are drawn to the array of 34, wherein the oligonucleotides are end capped with a 3' or 5' protective group for imparted exonuclease resistance.

Although McGall teaches that 2' modifications to the array oligonucleotides can enable the probes resistant to DNAase and RNAase, McGall does not specifically teach using a 3' or 5' protective group to protect against exonucleases.

King teaches using end-capped, capture probes for target hybridization, which differ from the uncapped oligonucleotide sequences in that the capped probes contain chemical moieties which are incorporated for the purpose of blocking the 3' and/or 5' terminal hydroxyl groups of the oligonucleotide chain. These blocking groups impart unique stability properties to the probe because they are no longer susceptible to degradation by a variety of exonucleases which are known to degrade oligonucleotide sequences (see *Use of End-Capped Oligonucleotides*).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the 3'/5' end-capping strategy as taught by King, to the endonuclease/acid stable oligonucleotide array of McGall (in light of Miller) and Lipshutz, because of the end-capping strategy provides a means of making the probes

also resistant to exonuclease degradation. Therefore, the invention as a whole was *prima facie* obvious at the time the invention was made.

Conclusion

8. No claims are allowable

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Jeffrey S. Lundgren whose telephone number is (703)

Application/Control Number: 09/408,761
Art Unit: 1631

Page 8

306-3221. The Examiner can normally be reached on Monday-Friday from 7:00 AM to 5:00 PM (EST).

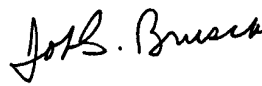
If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Michael Woodward, can be reached at (703) 308-4028.

Any inquiries of a general nature relating to this application should be directed to the Technology Center Receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed to Group 1631 using (703) 308-0294. Please notify the Examiner of incoming facsimiles prior to sending papers to the aforementioned fax number. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989).



Jeffrey S. Lundgren, Ph.D.



JOHN S. BRUSCA, PH.D
PRIMARY EXAMINER